PATENT COOPERATION TREATY From the INTERNATIONAL SEARCHING AUTHORITY To: DANIEL A. MONACO SEIDEL, GONDA, LAVORGNA, & MONACO, P.C. GONDA, LAVORGNA **SUITE 1800** & MONACO, P.O. TWO PENN CENTER PLAZA NOTIFICATION OF TRANSMITTAL OF PHILADELPHIA PA 19102 THE INTERNATIONAL SEARCH REPORT OR THE DECLARATION (PCT Rule 44.1) Date of Mailing 14 FEB 2000 lay/month/year) HACO, P.C. Applicant's or agent's file reference FOR FURTHER ACTION See paragraphs 1 and 4 below 6056-279 PC International application No. International filing date (day/month/year) PCT/US99/22756 **30 SEPTEMBER 1999** Applicant FRONTICELLI, CLARA The applicant is hereby notified that the international search report has been established and is transmitted herewith. Filing of amendments and statement under Article 19: The applicant is entitled, if he so wishes, to amend the claims of the international application (see Rule 46): The time limit for filing such amendments is normally 2 months from the date of transmittal of the international search report, however, for more details, see the notes on the accompanying sheet. Where? Directly to the International Bureau of WIPO 34, chemin des Colombettes 1211 Geneva 20, Switzerland Facsimile No.: (41-22) 740.14.35 For more detailed instructions, see the notes on the accompanying sheet. The applicant is hereby notified that no international search report will be established and that the declaration under Article 17(2)(a) to that effect is transmitted herewith. With regard to the protest against payment of (an) additional fee(s) under Rule 40.2, the applicant is notified that: the protest together with the decision thereon has been transmitted to the International Bureau together with the applicant's request to forward the texts of both the protest and the decision thereon to the designated Offices. no decision has been made yet on the protest; the applicant will be notified as soon as a decision is made. 4. Further action(s): The applicant is reminded of the following: Shortly after 18 months from the priority date, the international application will be published by the International Bureau. If the applicant wishes to avoid or postpone publication, a notice of withdrawal of the international application, or of the priority claim, must reach the International Bureau as provided in rules 90 bis 1 and 90 bis 3, respectively, before the completion of the technical preparations for international publication. Within 19 months from the priority date, a demand for international preliminary examination must be filed if the applicant wishes to postpone the entry into the national phase until 30 months from the priority date (in some Offices even later). Within 20 months from the priority date, the applicant must perform the prescribed acts for entry into the national phase before all designated Offices which have not been elected in the demand or in a later election within 19 months from the priority date or could not be elected because they are not bound by Chapter II. Name and mailing address of the ISA/US Authorized offic Commissioner of Patents and Trademarks (ANE CARLSON, PH.D. KAREN COCH Washington, D.C. 20231 (703) 308-0196 Telephone No. Facsimile No. (703) 305-3230

#### PATENT COOPERATION TREATY

From the INTERNATIONAL BUREAU

#### PCT

#### **NOTIFICATION CONCERNING** SUBMISSION OR TRANSMITTAL OF PRIORITY DOCUMENT

(PCT Administrative Instructions, Section 411)

MONACO, Daniel, A. Seidel, Gonda, Lavorgna & Monaco P.C. Suite 1800 Two Penn Center Plaza Philadelphia, PA 19102  ÉTATS-UNIS D'AMÉRIQUE  SEIDEL, GONDA, LAVORGNA, & MONACO, P.C.	То:	
Philadelphia, PA 19102 UEG Z 1999 ETATS-UNIS D'AMÉRIQUE SEIDEL GONDA LAYORGNA	Seidel, Gonda, Lavorgna 8 P.C. Suite 1800	Monaco E G E 1 V E
	Philadelphia, PA 1910211 ÉTATS-UNIS D'AMÉRIQU	SEIDEL, GONDA, LAYORGNA

IMPORTANT NOTIFICATION		
nternational filing date (day/month/year) 30 September 1999 (30.09.99)		
Priority date (day/month/year) 01 October 1998 (01.10.98)		

- The applicant is hereby notified of the date of receipt (except where the letters "NR" appear in the right-hand column) by the International Bureau of the priority document(s) relating to the earlier application(s) indicated below. Unless otherwise indicated by an asterisk appearing next to a date of receipt, or by the letters "NR", in the right-hand column, the priority document concerned was submitted or transmitted to the International Bureau in compliance with Rule 17.1(a) or (b).
- This updates and replaces any previously issued notification concerning submission or transmittal of priority documents.
- An asterisk(\*) appearing next to a date of receipt, in the right-hand column, denotes a priority document submitted or transmitted to the International Bureau but not in compliance with Rule 17.1(a) or (b), In such a case, the attention of the applicant is directed to Rule 17.1(c) which provides that no designated Office may disregard the priority claim concerned before giving the applicant an opportunity, upon entry into the national phase, to furnish the priority document within a time limit which is reasonable under the circumstances.
- The letters "NR" appearing in the right-hand column denote a priority document which was not received by the International Bureau or which the applicant did not request the receiving Office to prepare and transmit to the International Bureau, as provided by Rule 17.1(a) or (b), respectively. In such a case, the attention of the applicant is directed to Rule 17.1(c) which provides that no designated Office may disregard the priority claim concerned before giving the applicant an opportunity, upon entry into the national phase, to furnish the priority document within a time limit which is reasonable under the circumstances.

**Priority date** Priority application No. Country or regional Office Date of receipt or PCT receiving Office of priority document 01 Octo 1998 (01.10.98) 60/102,640 US 07 Dece 1999 (07.12.99)

The International Bureau of WIPO 34, chemin des Colombettes 1211 Geneva 20, Switzerland

Authorized officer

Olivia RANAIVOJAONA

Facsimile No. (41-22) 740.14.35

FRONTICELLI, Clara

Telephone No. (41-22) 338.83.38

TENT COL ERATION JUL 1 7 2000 JUL 1 7 2000 SEIDEL, GONDA, LAVORGNA, & MONACO, P.C. INTERNATIONAL PRELIMINARY EXAMINING AUTH EIDEL, GONDA, LAVORGNA & MONACO, P.C.

To: DANIEL A. MONACO SEIDEL, GONDA, LAVORGNA, & MONACO, **SUITE 1800** TWO PENN CENTER PLAZA

NOTIFICATION OF TRANSMITTAL OF INTERNATIONAL PRELIMINARY **EXAMINATION REPORT** 

(PCT Rule 71.1)

Date of Mailing (day/month/year) 2 JUL 2000

Applicant's or agent's file reference

PHILADELPHIA PA 19102

6056-279 PC

IMPORTANT NOTIFICATION

International application No.

International filing date (day/month/year)

Priority Date (day/month/year)

PCT/US99/22756

30 SEPTEMBER 1999

01 OCTOBER 1998

**Applicant** 

From the

TEMPLE UNIVERSITY OF THE COMMONWEALTH SYSTEM OF HIGHER EDUCATION

- ١. The applicant is hereby notified that this International Preliminary Examining Authority transmits herewith the international preliminary examination report and its annexes, if any, established on the international application.
- A copy of the report and its annexes, if any, is being transmitted to the International Bureau for communication 2. to all the elected Offices.
- 3. Where required by any of the elected Offices, the International Bureau will prepare an English translation of the report (but not of any annexes) and will transmit such translation to those Offices.

#### REMINDER 4.

The applicant must enter the national phase before each elected Office by performing certain acts (filing translations and paying national fees) within 30 months from the priority date (or later in some Offices)(Article 39(1))(see also the reminder sent by the International Bureau with Form PCT/IB/301).

Where a translation of the international application must be furnished to an elected Office, that translation must contain a translation of any annexes to the international preliminary examination report. It is the applicant's responsibility to prepare and furnish such translation directly to each elected Office concerned.

For further details on the applicable time limits and requirements of the elected Offices, see Volume II of the PCT Applicant's Guide.

Name and mailing address of the IPEA/US

Commissioner of Patents and Trademarks Box PCT

Washington, D.C. 20231

Facsimile No. (703) 305-3230

Authorized officer

KAREN COCHRANE CARLSON, PH.D.

Telephone No. (703) 308-0196

# PATENT COOPERATION TREATY

# **PCT**

#### INTERNATIONAL SEARCH REPORT

(PCT Article 18 and Rules 43 and 44)

Applicants of agents the reference		ation of Transmittal of International Search Report (ISA/220) as well as, where applicable, item 5 below.
International application No.	International filing date (day/month	/year) (Earliest) Priority Date (day/month/year)
PCT/US99/22756	30 SEPTEMBER 1999	01 OCTOBER 1998
Applicant FRONTICELLI, CLARA		
according to Article 18. A copy is bein This international search report consists	g transmitted to the International Bure	
1. Certain claims were found	unsearchable (See Box 1).	
2. Unity of invention is lacking	g (See Box II).	
international search was carr	contains disclosure of a nucleotide ed out on the basis of the sequence li filed with the international application furnished by the applicant separately if	
		a statement to the effect that it did not include matter sure in the international application as filed.
	the text is approved as submitted by t	••
5. With regard to the abstract,	the text is approved as submitted by t the text has been established, accordin	he applicant. g to Rule 38.2(b), by this Authority as it appears in one month from the date of mailing of this
6. The figure of the drawings to be p		
Figure No. 4	as suggested by the applicant.	None of the figures.
	because the applicant failed to sugges	t a figure.
	because this figure better characterize	s the invention.

#### INTERNATIONAL SEARCH REPORT

Inte	mational	application	No.
	T/US99/	22756	

A. CLASSIFICATION OF SUBJECT MATTER	- <del></del>	
IPC(6) :C07K 14/805; C07H 17/00; C12P 21/06	_	
US CL :530/385; 536/23.1; 435/69.6, 320.1, 252.3; 325; 514/ According to International Patent Classification (IPC) or to both r		
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B. FIELDS SEARCHED	hu danification much del	
Minimum documentation searched (classification system followed		
U.S. : 530/385; 536/23.1; 435/69.6, 320.1, 252.3; 325; 514/6		
Documentation searched other than minimum documentation to the none	extent that such documents are included	in the fields searched
Electronic data base consulted during the international search (na APS, Dialog	me of data base and, where practicable,	search terms used)
C. DOCUMENTS CONSIDERED TO BE RELEVANT		
Category* Citation of document, with indication, where app	propriate, of the relevant passages	Relevant to claim No.
X US 5,545,727 A (HOFFMAN et al) 13		23-24
Example 28; col. 22, lines 6-41; col. 1, y 5.	, ilies 44-45; col. 58, lines 1-	1-22
J.		1-22
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	<u>-</u>	
Further documents are listed in the continuation of Box C	. See patent family annex.	
Special categories of cited documents:	"T" later document published after the inte date and not in conflict with the appl	
"A" document defining the general state of the art which is not considered to be of particular relevance	the principle or theory underlying the	
*B* earlier document published on or after the international filing date	"X" document of particular relevance; the considered novel or cannot be considered.	
*L* document which may throw doubts on priority claim(s) or which is	when the document is taken alone	поле вы вичения с зкер
cited to establish the publication date of another citation or other special reason (as specified)	"Y" document of particular relevance; the considered to involve an inventive	
"O" document referring to an oral disclosure, use, exhibition or other means	combined with one or more other such being obvious to a person skilled in	h documents, such combination
*P* document published prior to the international filing date but later than the priority date claimed	*&' document member of the same paten	
Date of the actual completion of the international search	Date of mailing of the international sea	arch report
18 JANUARY 2000	14 168	(000
Name and mailing address of the ISA/US Commissioner of Patents and Trademarks	Authorized officer	Clin for
Box PCT Washington, D.C. 20231	KAREN COCHRANE CARLSON	PH.D.
Facsimile No. (703) 305-3230	Telephone No. (703) 308-0196	

Form PCT/ISA/210 (second sheet)(July 1992)\*

### PATENT COOPERATION TREATY

## **PCT**

#### INTERNATIONAL PRELIMINARY EXAMINATION REPORT

(PCT Article 36 and Rule 70)

Applicant's or agent's file reference 6056-279 PC	FOR FURTHER ACTION	See Notification of Transmittal of International Preliminary Examination Report (Form PCT/IPEA/416)
International application No.	International filing date (day/m	nonth/year) Priority date (day/month/year)
PCT/US99/22756	30 SEPTEMBER 1999	01 OCTOBER 1998
International Patent Classification (IPC) Please See Supplemental Sheet.	or national classification and IPG	'C
Applicant TEMPLE UNIVERSITY OF THE CO	MMONWEALTH SYSTEM OF	F HIGHER EDUCATION
Examining Authority and is  2. This REPORT consists of a  This report is also accombeen amended and are the	transmitted to the applicant a total of sheets. upanied by ANNEXES, i.e., shee	ets of the description, claims and/or drawings which have eets containing rectifications made before this Authority. Instructions under the PCT).
These annexes consist of a to	otal of sheets.	
IV Lack of unity of  V X Reasoned stateme citations and explanation of the complete	ort  nt of report with regard to not invention  nt under Article 35(2) with regard to not under	ovelty, inventive step or industrial applicability gard to novelty, inventive step or industrial applicability; ment
Date of submission of the demand 31 MARCH 2000		e of completion of this report
Name and mailing address of the IPEA  Commissioner of Patents and Trade Box PCT Washington, D.C. 20231	marks K	MORIZED STORE CARLSON PH.D.
Facsimile No. (703) 305-3230	Telep	phone No. (703) 308-0196

#### INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No.

PCT/US99/22756

I. B:	asis of the	report		
1. With	regard to th	e elements of the interna	ational application:*	
$\bar{\mathbf{x}}$	_	ational application as		
=	the descri	• •		
х	pages			as originally filed
	pages	NONE		
	pages		, filed with the letter of	
	Pug03		, ,	
$\mathbf{x}$	the claims	<b>3</b> :		
بنا	pages	27-30		, as originally filed
	pages	NONE	, as amended (together with any s	•
	pages	NONE		
	pages	NONE	, filed with the letter of	
X	the drawn			
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	pages	NONE	, filed with the letter of	
		11.41.	1	
X	the sequer	nce listing part of the	description:	an animinally filed
			, filed with the letter of	
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	the langua	age of publication of	urnished for the purposes of international search (the international application (under Rule 48.3(b)). mished for the purposes of international preliminary exa	
	or 55.3).	ge (A die dinbidden ita	inside to the purposes of the national premium, ex-	inimiation (taker reales 55.2 take
			or amino acid sequence disclosed in the international dout on the basis of the sequence listing:	l application, the international
	contained	in the international	application in printed form.	
	filed toge	ther with the internat	tional application in computer readable form.	
	furnished	subsequently to this	Authority in written form.	
	furnished	subsequently to this	Authority in computer readable form.	
	The states	ment that the subseque	ently furnished written sequence listing does not go b	beyond the disclosure in the
<u> </u>	_	nal application as filed		a maile a community of the
	been funi		on recorded in computer readable form is identical to the	e writen sequence listing has
4. X	The ame	ndments have resulte	ed in the cancellation of:	
	X the	description, pages	NONE	
		claims, Nos.		
Ì		drawings, sheets#ig		
5. [	٦		(some of) the amendments had not been made, since the	ay have been considered to as
			s indicated in the Supplemental Box (Rule 70.2(c)).**	y three occur considered to go
in	placement sh	eets which have been fu	rnished to the receiving Office in response to an invitation d are not annexed to this report since they do not con	
	-	ent sheet containing su	ch amendments must be referred to under item I and	annexed to this report.



International application No.

PCT/US99/22756

statement			
Novelty (N)	Claims	1-24	Y
	Claims	NONE	N
Inventive Step (IS)	Claims	1-24	Y
	Claims	NONE	N
Industrial Applicability (IA)	Claims	1-24	Y
	Claims	NONE	N
 NONE			
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International application No.

PCT/US99/22756

Supplemental	Box		

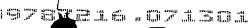
(To be used when the space in any of the preceding boxes is not sufficient)

Continuation of: Boxes I - VIII

Sheet 10

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The International Patent Classification (IPC) and/or the National classification are as listed below: IPC(7): C07K 14/805; C07H 17/00; C12P 21/06 and US CI.: 530/385; 536/23.1; 435/69.6, 320.1, 252.3; 325; 514/6





### WORLD INTELLECTUAL PROPERTY ORGANIZATION International Bureau



#### INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(51) International Patent Classification 6: C07K 14/805, C07H 17/00, C12P 21/06

A1

(11) International Publication Number:

WO 00/18802

(43) International Publication Date:

6 April 2000 (06.04.00)

(21) International Application Number:

PCT/US99/22756

(22) International Filing Date:

30 September 1999 (30.09.99)

(30) Priority Data:

60/102,640

1 October 1998 (\$\displays{1}.10.98) US

(71) Applicant (for all designated States except UNIVERSITY - OF THE COMMONWEALTH SYSTEM OF HIGHER EDUCATION [US/US]; Broad Street and Montgomery Avenue, Philadelphia, PA 19122 (US).

(72) Inventor; and

(75) Inventor/Applicant (for US only):, FRONTICELLI, Clara [US/US]; 11514 Pebble Creek, Timonium, MD 21093 (US).

(74) Agent: MONACO, Daniel, A.; Seidel, Gonda, Lavorgna & Monaco, P.C., Suite 1800, Two Penn Center Plaza, Philadelphia, PA 19102 (US).

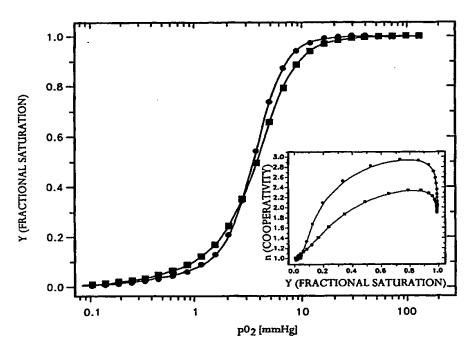
(81) Designated States: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZA, ZW, ARIPO patent (GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW), Eurasian patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European patent (AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG).

#### Published

With international search report.

Before the expiration of the time limit for amending the claims and to be republished in the event of the receipt of amendments.

(54) Title: POLYMERIC HEMOGLOBIN MUTANTS



#### (57) Abstract

Human  $\beta$ -globin mutant polypeptides comprise the amino acid sequence of normal human  $\beta$ -globin modified by (i) the substitution or deletion of Cys at positions (93) and (112), and (ii) the substitution of a Cys for a non-Cys amino acid at one other position in the polypeptide, preferably Ser at position (9). Modified human hemoglobins containing this or other  $\beta$ -globin mutations, and/or an  $\alpha$ -globin mutation, are provided, as well as polymers of such modified hemoglobins. Nucleic acids, vectors and transformed host cells for producing the  $\beta$ -globin mutants are provided.

#### FOR THE PURPOSES OF INFORMATION ONLY

Codes used to identify States party to the PCT on the front pages of pamphlets publishing international applications under the PCT.

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EE	Estonia	LR	Liberia	SG	Singapore		

### INTERNATIONAL SEARCH REPORT

International application No.
PCT/US99/22756

A. CLASSIFICATION OF SUBJECT MATTER						
IPC(6) :C07K 14/805; C07H 17/00; C12P 21/06 US CL :530/385; 536/23.1; 435/69.6, 320.1, 252.3; 325; 514/6						
According to International Patent Classification (IPC) or to both	national classification and IPC					
B. FIELDS SEARCHED						
Minimum documentation searched (classification system follower	d by classification symbols)					
U.S. : 530/385; 536/23.1; 435/69.6, 320.1, 252.3; 325; 514/	6					
Documentation searched other than minimum documentation to the	e extent that such documents are included in the fields searched					
Electronic data base consulted during the international search (n. APS, Dialog	ame of data base and, where practicable, search terms used)					
C. DOCUMENTS CONSIDERED TO BE RELEVANT						
Category* Citation of document, with indication, where ap	propriate, of the relevant passages Relevant to claim No	0.				
X US 5,545,727 A (HOFFMAN et al) 1: Example 28; col. 22, lines 6-41; col. 1	• • •					
Y 5.	1-22					
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Further documents are listed in the continuation of Box C	See patent family annex.	,				
Special categories of cited documents:	"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand					
"A" document defining the general state of the art which is not considered to be of particular relevance	the principle or theory underlying the invention					
"E" carlier document published on or after the international filing date	"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step					
"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other	when the document is taken alone  "Y" document of particular relevance: the claimed invention cannot be					
special reason (as specified)  *O* document referring to an oral disclosure, use, exhibition or other	"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination	3				
means  "P" document published prior to the international filing date but later than	being obvious to a person skilled in the art					
the priority date claimed	Y=					
Date of the actual completion of the international search 18 JANUARY 2000	Date of mailing of the international search report  14 FEB 2000					
Name and mailing address of the ISA/US	Authorized officer					
Commissioner of Patents and Trademarks Box PCT Washington, D.C. 20231	KAREN COCHRANE CARLSON, PH.D.					
Facsimile No. (703) 305-3230	Telephone No. (703) 308-0196					

Form PCT/ISA/210 (second sheet)(July 1992)\*

### PAIENT COOPERATION TREATY

From the INTERNATIONAL BUREAU

PCT	То:
NOTIFICATION OF ELECTION (PCT Rule 61.2)	Assistant Commissioner for Patents United States Patent and Trademark Office Box PCT Washington, D.C.20231 ETATS-UNIS D'AMERIQUE
Date of mailing (day/month/year) 16 May 2000 (16.05.00)	in its capacity as elected Office
International application No. PCT/US99/22756	Applicant's or agent's file reference 6056-279 PC
International filing date (day/month/year) 30 September 1999 (30.09.99)	Priority date (day/month/year) 01 October 1998 (01.10.98)
Applicant FRONTICELLI, Clara	
The designated Office is hereby notified of its election made:  In the demand filed with the International Preliminary Examining Authority on:  31 March 2000 (31.03.00)  in a notice effecting later election filed with the International Bureau on:	
2. The election X was was was not made before the expiration of 19 months from the priority date or, where Rule 32 applies, within the time limit under Rule 32.2(b).	
The International Bureau of WIPO 34, chemin des Colombettes 1211 Geneva 20, Switzerland	Authorized officer  Juan Cruz

Telephone No.: (41-22) 338.83.38

Form PCT/IB/331 (July 1992)

Facsimile No.: (41-22) 740.14.35